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ORIGINAL ARTICLE

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Transplantation of infant en bloc kidneys into paediatric recipients

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Abstract En bloc renal transplantation (EBT) from infant donors is an option for children with end-stage renal failure. Owing to potential complications, EBT is not performed in all paediatric nephrology centres. We evaluated the perioperative and long-term course of five children undergoing EBT. Primary diagnosis was atypical (diarrhoea-negative) haemolytic uraemic syndrome (n=2), interstitial nephropathy (two siblings) and branchio-oto-renal syndrome (n=1). Recipient and donor ages ranged between 5.9 and 11.1 years and 0.3 and 2.5 years, respectively. Follow-up time after EBT was 2.1–13.2 years. Perioperative complications included (1) a renal artery thrombosis, with immediate intraoperative reconstruction and primary non-functioning of the graft, with recovery after 10 days, and (2) a vesico-ureteric obstruction, successfully managed with temporary insertion of a JJ-catheter. All grafts had good long-term function. Absolute glomerular filtration rate (GFR; millilitres/minute) increased in all patients, whereas relative GFR (millilitres/minute per 1.73 m^2 body surface area) remained stable during the follow-up period in all but one. Kidney size increased significantly, with maximal growth during the first year after EBT; magnetic resonance imaging (MRI) showed normal structure and vasculature. EBT is a safe and effective option for young children with end-stage renal failure. Absolute GFR and graft size increase and adapt to the children's growing body mass.

Keywords Infant en bloc renal transplantation · Glomerular filtration rate · Transplantation · Kidney · Long-term outcome

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Introduction

Paediatric renal transplantation is the treatment of choice for children with end-stage renal failure. The success of this procedure has created an increasing shortage of donor organs, as the number of potential kidney transplant recipients has grown faster than the number of available donor kidneys. This imbalance has led to expansion of the criteria for the donor pool, including paediatric donors under the age of 5 years. However, the use of kidney(s) from young paediatric donors, transplanted as single-kidney [1] or as infant en bloc transplantation (EBT) has been controversial discussed [2, 3, 4, 5]. A high complication rate was reported after EBT in adult recipients, e.g. graft thrombosis, urological problems and early rejection [1, 2, 3], although graft survival and graft function were favourable [4, 5, 6, 7, 8, 9]. This high complication rate was observed not only in adults but also in the few paediatric recipients undergoing EBT. Thus, the role of EBT in paediatric recipients remained highly controversial [10, 11].

Kidneys from paediatric donors transplanted into the growing child showed a better long-term functional adaptation than did adult-donor kidneys [12, 13]. In contrast to adult grafts, absolute glomerular filtration rate (GFR) and kidney size increased in children receiving paediatric grafts in relation to body growth [12, 13, 14, 15, 16].

We report on a small series of five children undergoing EBT from young donors below the age of 30 months. All grafts survived, and absolute GFR and kidney size increased in relation to the growing body mass.

Patients and methods

Since 1970, 132 children and adolescents below 20 years of age have undergone transplantation at the University Children's Hospital in Zurich. Five of them underwent EBT between 1992 and 2003. Primary diagnosis was atypical (diarrhoea-negative) haemolytic uraemic syndrome (*n*=2), familial interstitial nephropathy (two siblings) and branchio-oto-renal syndrome (*n*=1). Recipient and donor ages ranged from 5.9 to 11.1 years and 0.3 to 2.5 years, respectively. Informed consent was given by all parents.

Patients received triple immunosuppressive therapy: cyclosporine A (aiming at a trough level of 180–250 ng/ml for the first 6 months and 80–120 ng/ml thereafter), azathioprine (1 mg/kg per day) and prednisone, in patients A, B and C. Patients D and E were given mycophenolate mofetil (1,200 mg/m^2 body surface area per day) instead of azathioprine. The initial prednisone dosage was 1 mg/kg per day, which was then tapered to alternate days after 6 months (5 mg/m^2); prednisone was successfully withdrawn after 1 year in patients A, D and E.

All grafts were ABO compatible, and crossmatch was negative. Patients A (A, B, DR) and B (A, DR) had three and two matches, respectively; there was a complete HLA-mismatch in patients C, D and E.

Surgical procedure in the donor was dissection of the suprarenal aorta and inferior vena cava above the junction with the renal vessels. The lower abdominal aorta and vena cava were removed en bloc, together with the two kidneys, after ligation of the lumbar vessels and the inferior mesenteric artery. Both the infrarenal aorta and cava were closed by ligature two-to-three cm caudal to the junction with the renal vessels. The suprarenal ends of the aorta and cava were left open and used for end-to-side anastomosis to the recipient's arteria and vena iliaca in patients A, B and E and to the recipient's aorta and vena cava in patients C and D. Implantation of the ureter was performed by an extravesical technique. In patients A, B and C a catheter was inserted transcutaneously between pyelon and bladder, whereas a JJ-catheter was inserted between pyelon and bladder in patients D and E. All catheters were removed 3 weeks after transplantation. Anticoagulation prophylaxis with intravenously administered heparin (10 U/kg body weight per hour) was started at the beginning of the operation and was continued for 14 days. Mannitolum (20%, 2 ml/kg body weight) was injected during the anastomosis of donor's and recipient's vessels.

Estimated GFR was assessed either by the Schwartz formula or Cr-EDTA clearance [17]. Kidney size and growth were measured by ultrasound. In addition, repeated 24-h ambulatory blood pressure measurement (24-h-ABPM) and magnetic resonance imaging (MRI) with contrast-enhanced angiography (at the most recent appointment in four patients) were performed. Anthropometric data were compared with the norm for age and gender of Swiss children [18].

Results

Perioperative course

Clinical data of donors and recipients are summarized in Tables 1 and 2. The course of *patient A* was uneventful. *Patient B* experienced renal artery thrombosis during the operation, with immediate intraoperative reconstruction. In spite of the young age of the recipient, 5.9 years, the donor's vessels had been anastomosed to the recipient's common iliac artery and vein. Because primary non-functioning of the graft occurred, the immunosuppressive treatment was switched on day 2 from cyclosporin A to anti-thymocyte globulin (ATG, Fresenius, 3 mg/kg body weight per day) for 10 days, resulting in full recovery of renal function. In *patient C*, a JJ-catheter was inserted 2 months after EBT because of a vesico-ureteric obstruction of the cranial ureter. Six months later the catheter was removed, and drainage remained normal. *Patients C, D and E* experienced a single episode of histologically proven acute rejection 6 weeks, 3 weeks and 4 weeks after EBT, respectively. Treatment consisted of six (*patient C*) and three (*patients D, E*) methylprednisolone-pulses (500 mg/m^2 per day, intravenously) with renal function (plasma creatinine) returning to baseline in all patients.

Table 1 Clinical data of recipients and donors at EBT (*m* male, *f* female, *CIT* cold ischaemia time)

Patient (gender)	Age of donor (months)	CIT (h)	Age of recipient (years)	Height, cm (percentile)	Weight, kg (percentile)
A (m)	24	26	9.1	133 (50)	31 (75)
B (f)	8	22	5.9	104 (<3)	16 (3)
C (m)	4	15	9.1	125 (3)	25 (10)
D (f)	20	18	5.9	106 (3)	16 (3)
E (f)	30	16	11.1	133 (10)	26 (3)

Table 2 Clinical follow-up data of recipients (1 year after EBT and most recent examination). GFR is in millilitres/minute per 1.73 m^2. (*m* male, *f* female)

Patient (gender)	Follow-up (years)	Height, cm (percentile)	Weight, kg (percentile)	Casual blood pressure on treatment (mmHg)	GFR[a] (Schwartz formula)	GFR[a] (Cr-EDTA-clearance)
A (m)	1	144 (75)	38 (90)	128/80	71	Not done
	13.2	192 (97)	91(>97)	138/82	51	28
B (f)	1	112 (3)	23 (50)	95/70	63	80
	8.7	161 (25)	52 (50)	122/70	73	Not done
C (m)	1	131 (10)	29 (25)	112/78	78	83
	7.1	175 (50)	72 (90)	120/63	76	Not done
D (f)	1	110 (3)	19 (10)	127/86	90	85
	4.6	137 (10)	28 (10)	100/61	94	110
E (f)	1	142 (10)	35 (25)	116/78	86	Not done
	2.1	154 (25)	41 (25)	107/61	89	106

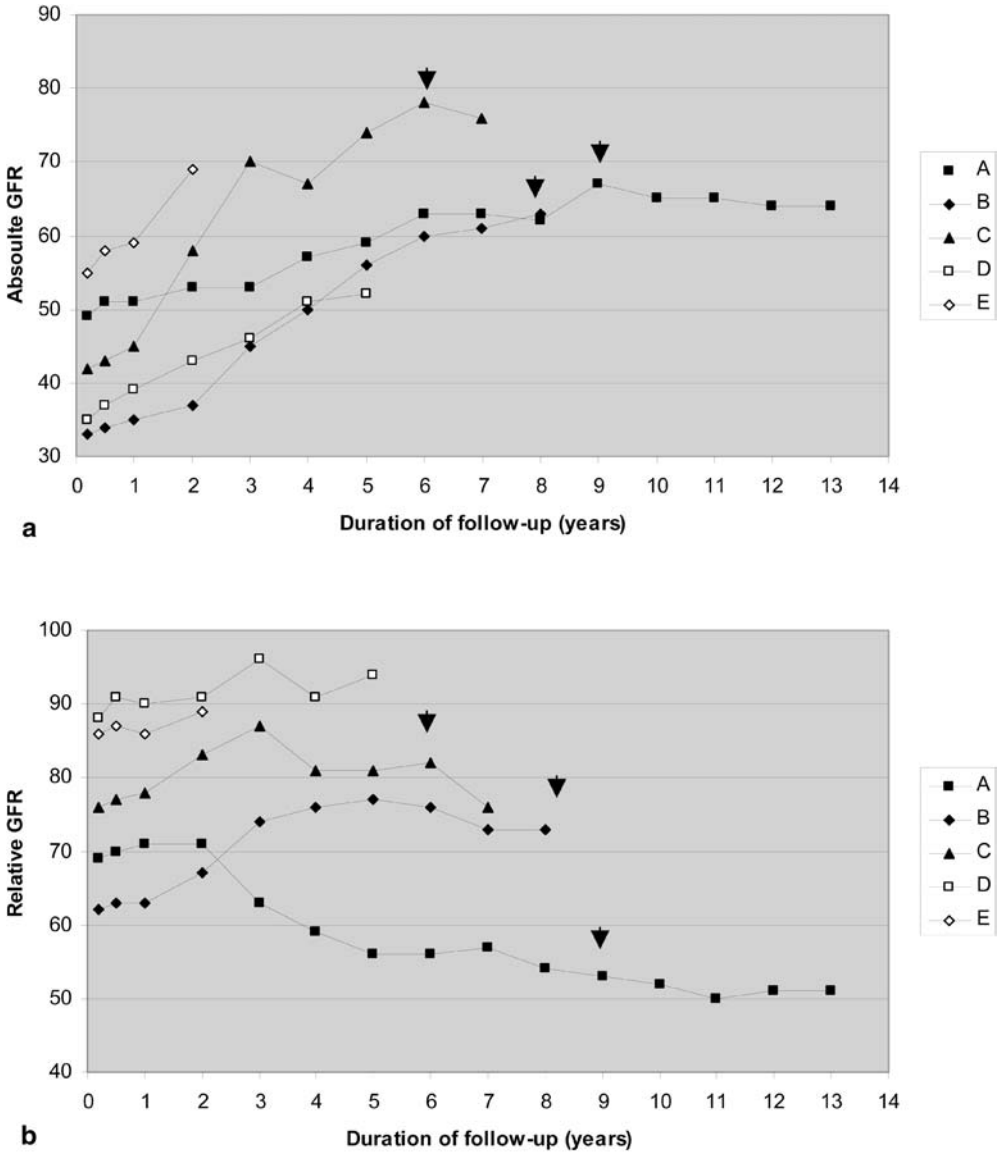

Fig. 1 **a** Absolute GFR (Schwartz formula) in millilitres/minute during the follow-up period. *Arrowheads* final height reached. **b** Relative GFR (Schwartz formula) in millilitres/minute per 1.73 m^2 body surface area during the follow-up period. *Arrowheads* final height reached

Long-term course

Long term follow-up times ranged from 2.1 years to 13.2 years. All patients had good graft function. Absolute GFR (millilitres/minute) increased in all patients and reached maximum level at the end of the adolescents' linear growth in *patients A, B and C* (Fig. 1a). Relative GFR (millilitres/minute per 1.73 m^2 body surface area) remained stable during the follow-up period in *patients B, C, D and E* (Fig. 1b). Relative GFR decreased in *patient A*, in accordance with his prominent body mass: weight (91 kg), height (191 cm) and body surface area (2.0 m^2). Four patients were hypertensive, as assessed by both casual blood pressure and 24-h-ABPM (mean arterial blood pressure >95th percentile), and required antihypertensive medication. None had proteinuria. Urinary tract infection occurred in *patients B, C and E*; a voiding cystogram revealed vesico-ureteric reflux in *patient E*.

Kidney size and growth

Maximal growth of the transplanted kidneys occurred during the first year after EBT. The kidneys had reached their maximum size at the end of linear growth in *patients A, B and C*. The most recent measurement of the cranial and caudal kidneys showed normal size for age and weight in *patients A, B, D and E* [19] (Fig. 2), whereas the size of both kidneys was below the fifth percentile in *patient C* [19]. MRI, performed in four patients, showed normal structure and vasculature in all (data not shown).

Discussion

Our series of EBT in young paediatric recipients has shown a favourable long-term outcome, demonstrating

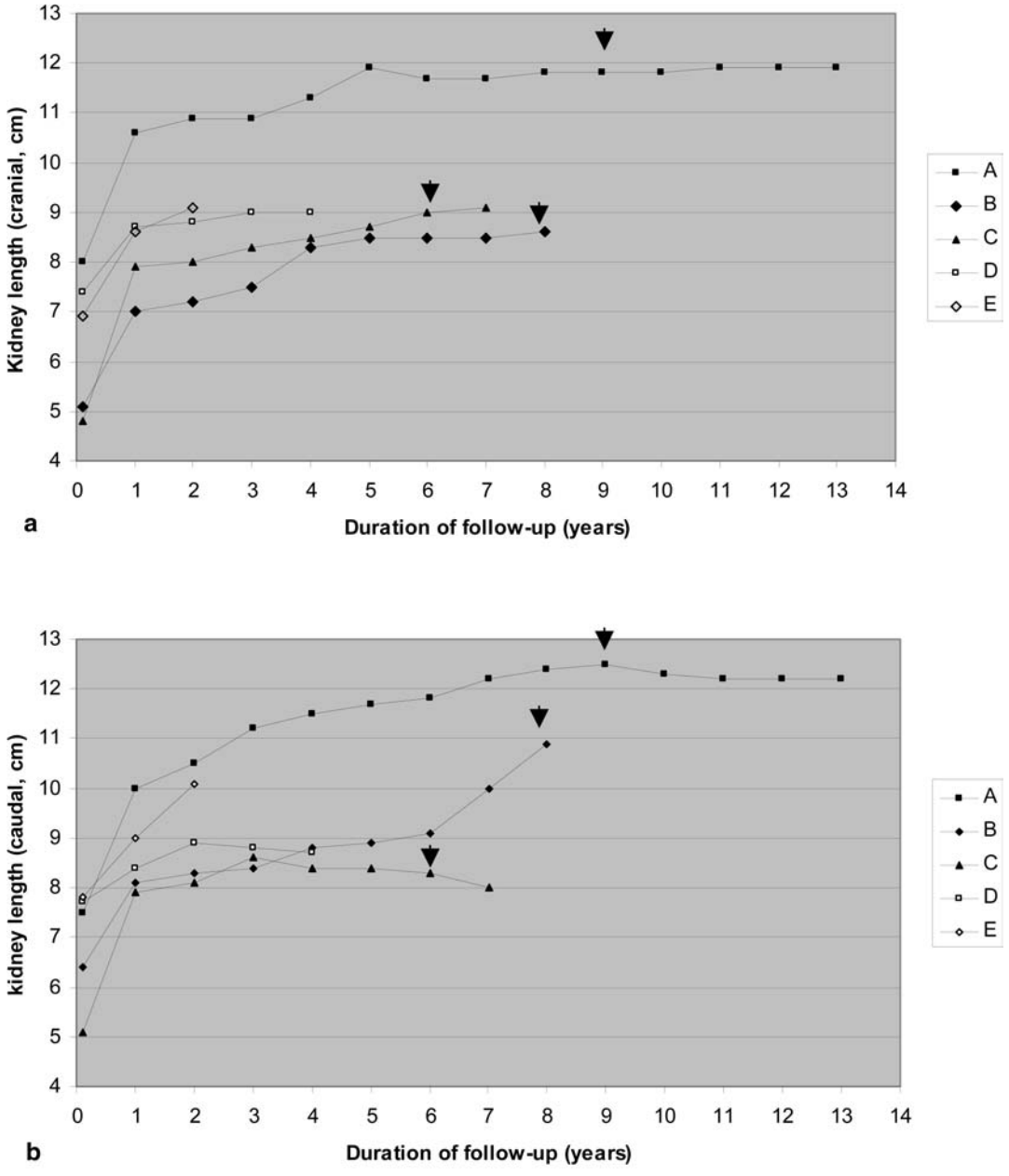

Fig. 2 **a** Length (centimetres) of cranial kidney during the follow-up period. *Arrowheads* final height reached. **b** Length (centimetres) of caudal kidney during the follow-up period. *Arrowheads* final height reached

that EBT is an option not only for adult but also for paediatric recipients.

The few perioperative vascular and urological complications were successfully managed, with a minimum of interventions. The anticoagulation therapy of patients during and after renal transplantation might have contributed to the favourable outcome. The intraperitoneal positioning of the vascular anastomoses to the distal aorta and inferior vena cava has been shown to be a feasible and successful technique in children who receive a transplant while less than 5 years of age [19]. In children undergoing EBT this procedure needs also to be considered in older children, as patient B sustained an intraoperative renal arterial thrombosis at the age of 5.9 years. The large diameters of the distal aorta and inferior vena cava, compared to those of the iliacal vessels, might prevent technical failures and subsequent graft thrombosis. In addition, repeated ultrasound imaging is required after EBT to focus on ureteric dilatation secondary to vesico-ureteric obstruction.

Absolute GFR increased in relation to body growth in all recipients, resulting in a stable relative GFR. Consistent with absolute GFR, kidney size increased after EBT, and growth rate was highest during the first year after EBT. The most recent size of nine out of ten kidneys was normal compared with that of age-related healthy controls

[20]. In particular, five out of the six kidneys of the three patients who had reached final linear growth were also normal for age and body size [20]. These observations are consistent with other studies confirming that kidney(s) from paediatric donors have the potential to increase glomerular function in relation to body growth and therefore to adapt to the growing child [12, 13, 14, 15, 16]. In contrast, adult-donor kidneys transplanted into children down-regulate their glomerular function immediately in the perioperative period in relation to body size of paediatric recipients and lack the capacity to increase its function according to subsequent body growth in children [12, 13]. These results confirm the notion that kidney(s) from paediatric donors should be allocated with higher priority to paediatric recipients [21].

In summary, en bloc renal transplantation from infant donors was a safe and effective option for young children with end-stage renal failure. Absolute GFR and kidney size adapted to increasing size and body mass of growing children, leading to excellent long-term function.

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